

# Trend Watch



## Alzheimer's Therapies

by Elisa F. Cascade and Amir H. Kalali, MD

**Featuring expert commentary from**  
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**ABSTRACT:** This article investigates the role that psychiatrists play in the prescription of Alzheimer's disease therapies and the similarities and differences in treatment approach when compared to primary care physicians and neurologists. Psychiatrists account for 7.6 percent of new patient starts on Alzheimer's disease therapies. Similar to other prescribers, over 75 percent of product use by psychiatrists is for two diagnoses: 294—Other Organic Psychiatric Condition and 331—Cerebral Degeneration. The primary difference between

psychiatrists and other prescribers is in the concomitant use of antipsychotics, antidepressants, and seizure disorder therapies. Specifically, psychiatrists use antipsychotics, antidepressants, and antiepileptics in combination with Alzheimer's disease therapies in 27 percent, 12 percent, and nine percent of treatment regimens, respectively. In contrast, these drug classes are used concomitantly in less than five percent of treatment regimens for patients treated by neurologists and primary care physicians. An expert commentary is provided.

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**KEY WORDS:** Alzheimer's disease, dementia, antipsychotics, antidepressants, antiepileptics, primary care, neurology

### INTRODUCTION

This article investigates the role that psychiatrists play in the prescription of Alzheimer's disease therapies and similarities and differences in treatment approaches when compared to primary care physicians and neurologists.

### METHODS

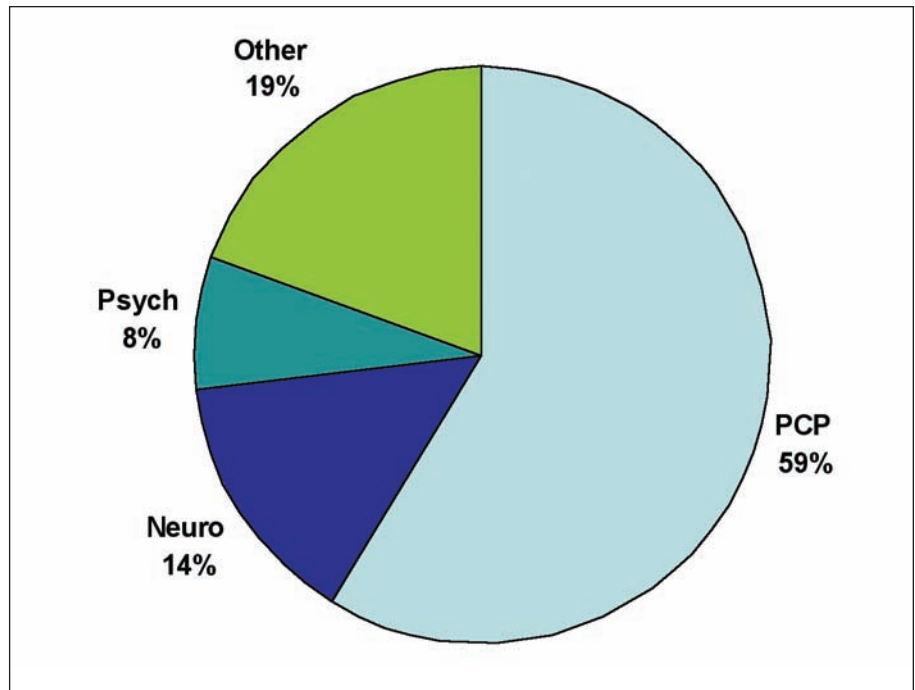
We obtained data from the following sources: 1) new patient starts on Alzheimer's disease therapies (USC Class 20400) by

specialty from Vector One National (VONA), which captures nearly half of all prescription activity in the US and 2) annual data from Verispan's Prescription Drug & Diagnosis Audit (PDDA) database by specialty regarding most common uses of Alzheimer's disease therapies and classes used in combination with Alzheimer's disease therapies. PDDA captures data on disease state and associated therapy from 3,100 office-based physicians representing 29 specialties across the United States.

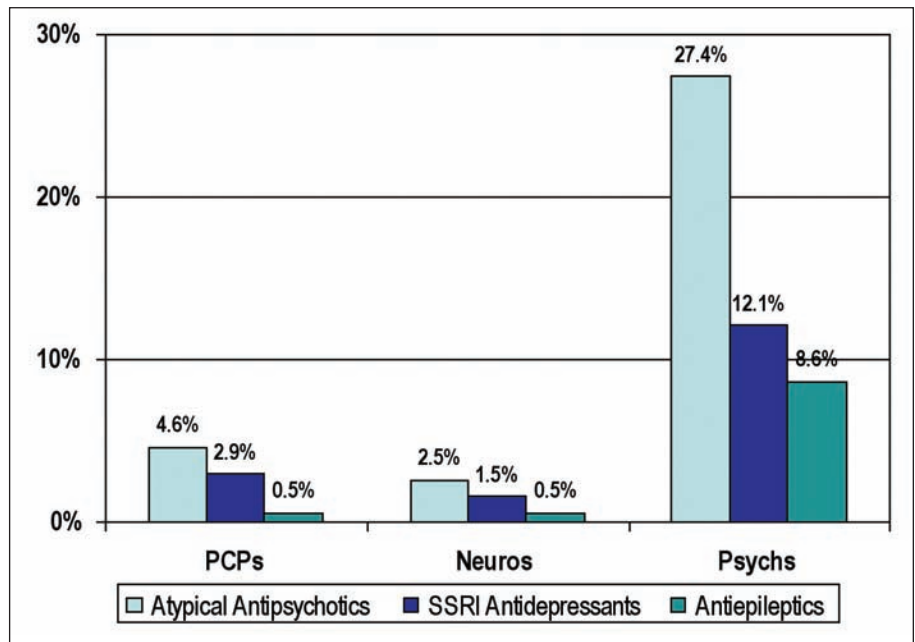
## RESULTS

Figure 1 displays new patient starts on Alzheimer's disease therapies by physician specialty. As seen in Figure 1, primary care physicians account for slightly more than 50 percent of new patient starts, followed by neurologists (14%) and psychiatrists (8%). Similar to other prescribers, over 75 percent of product use by psychiatrists is for two ICD-9 diagnoses codes: 294—other organic psychiatric condition and 331—cerebral degeneration.

Despite the fact psychiatrists use Alzheimer's disease therapies to treat patients with a similar diagnosis as compared to primary care physicians and neurologists, psychiatrists more commonly use antipsychotics, antidepressants, and antiepileptics in combination with the Alzheimer's disease therapies. As displayed in Figure 2, psychiatrists use antipsychotics, antidepressants, and antiepileptics in combination in 27 percent, 12 percent, and nine percent of treatment regimens, respectively. In contrast, these drug classes are used concomitantly in less than five percent of Alzheimer's disease treatment regimens for patients treated by neurologists and primary care physicians.



**FIGURE 1.** New Patient Starts on Alzheimer Therapy (20400) by Specialty  
Source: Verispan VONA, New Patient Starts USC 20400 Alzheimer's Disease Therapies, June 2006 - May 2007.



**FIGURE 2.** Agents Used in Combination with Alzheimer's Disease Therapies by Specialty  
Source: Verispan PDDA, classes used in combination with USC 20400 - Alzheimer's Disease Therapies, April 2006 - March 2007.

**EXPERT COMMENTARY****by Edmund Howe, MD, JD**

There are a number of possible reasons why psychiatrists prescribe antipsychotics, antidepressants, and antiepileptics in combination with Alzheimer's disease therapies more often than primary care doctors and neurologists.

On the one hand, these differences may reflect optimal practice. Perhaps primary care physicians and neurologists are using a "tiered" approach to treating dementia patients, which is clinically the state of the art.<sup>1</sup> This approach involves physicians treating patients within the scope of their primary expertise and then referring them to specialists when that scope is exceeded. Accordingly, primary care doctors and neurologists might refer dementia patients to psychiatrists or at least collaborate with them once their expertise is exceeded. Psychiatrists can then individualize patient care so that each patient benefits as much as possible.

Psychiatrists may be willing to take greater risks than their primary care and neurology counterparts by offering off-label medication. It is not surprising that psychiatrists would be more willing than non-psychiatrists to use these classes of drugs in an off-label manner in dementia patients, primarily because psychiatrists are more familiar with these drugs; after all, psychiatrists use these drugs regularly in their practices to treat other mentally ill patient populations.

These practice differences could also suggest that when it comes to medication, the needs of dementia patients are not being optimally met. Perhaps primary care doctors and neurologists are not sufficiently recognizing the behavioral and psychological needs of dementia patients and, as a result, are not sufficiently collaborating with

psychiatrists in order to become more comfortable using any or all of these medications. At worst, the Trend Watch data could reflect that groups of physicians are still treating dementia patients based on an outdated paradigm; these doctors may feel therapeutic nihilism as opposed to approaching these patients with optimal initiative at all stages of this disease.<sup>2</sup>

What should be done to eliminate these discrepancies of practice? A first response would be to establish comprehensive evidence-based guidelines on the treatment of AD and then fully educate all physicians who treat this patient population. This already to some extent is being done.<sup>3</sup>

The practice of using evidence-

of psychotropic medication may be justified or preferable in certain subgroups of patients. Citrome reports, for instance, on a study involving "very frail patients with dementia," whose mean was age 86. Their death rate, if not taking antipsychotics, was actually increased.<sup>5</sup>

And when it comes to antidepressants in the treatment of dementia patients who are depressed, evidence-based data have suggested that antidepressants are quite limited in dementia patients.<sup>6</sup> A more recent meta-analysis suggests, however, that this may not be the case.<sup>7</sup> Data also suggest that early treatment of depression may help these patients' underlying AD symptoms indirectly, if not directly.<sup>8</sup> For example, if a

**Empirical data has shown that collaboration between the groups of doctors can improve patient treatment within our present health system.<sup>16</sup> The need for this collaboration will increase as the population with AD grows.**

based guidelines will not, however, resolve the question of when to use medications off-label. For example, a recent study suggests that patients with problems in executive functioning impairment due to vascular dementia may respond exceptionally well to high doses of sertraline (200mg). This presumably is due to sertraline's effect on the dopamine system at this higher dose.<sup>4</sup> Should a physician prescribe this treatment to a patient who seems to warrant it?

Cascade and Kalali find, not surprisingly, that psychiatrists will often use antipsychotic drugs to treat patients with dementia, despite the serious risks, including an increased risk of death.<sup>5</sup> However, off-label usage

dementia patient is depressed, his depression may increase both his and his caregiver's stress. Stress, if not the depression, can then exacerbate the AD symptoms.<sup>9</sup>

What about the use of anticonvulsants? Findings have suggested that anticonvulsants have an important place in treating patients with AD who are agitated and aggressive.<sup>10</sup> Other recent studies have made this less clear.<sup>11,12</sup>

When considering off-label usage of medication, it is especially important to consider why it might be ethically preferable for not only psychiatrists but all doctors to go beyond or even against evidence-based practices, as long as they have the informed consent of the patients and their

families. Evidence-based practices are based on objective criteria, such as the extent to which drugs extend or shorten patients' lives. The quality of patients' lives, however, may be of comparable importance, and what this quality consists of varies from patient to patient.

The quality of the life of patients with AD may be greatly impaired, particularly in the last stages of the disease. Therefore, in the more extreme cases, it may be justifiable or even morally obligatory for physicians to do whatever they can to try to enhance or restore quality of life to these patients.<sup>13</sup> Even when these patients have severe dementia, they still benefit significantly from medications that can reduce their anxiety or agitation,<sup>14</sup> because emotional problems such as these may require loved ones to place these patients in nursing homes, and this may reduce their quality of life.<sup>15</sup>

In sum, this Trend Watch finds differences in the extent to which psychiatrists, primary care doctors, and neurologists use antipsychotics, antidepressants, and anticonvulsants when treating patients with AD. These differences may reflect that these groups are treating these patients, according to the differing severity of illness, as they ideally should, with the primary care doctors and neurologists referring the more emotionally disturbed patients to psychiatrists for specialized care. The differences also may reflect that the behavioral and psychological needs of AD patients are not being optimally met.

Empirical data has shown that collaboration between the groups of doctors can improve patient treatment within our present health system.<sup>16</sup> The need for this collaboration will increase as the population with AD grows. In the near future, it may be that our basic approach to diagnosing AD radically changes as the need for more specialized doctors grows.<sup>17</sup> Physicians

making AD diagnoses may need special expertise in assessing lab findings, such as structural neuroimaging with MRI and molecular neuroimaging with PET.<sup>18</sup> This change may be necessary to help us distinguish different subtypes of AD, and the need for collaboration will be even greater.

## REFERENCES

1. Draper B, Brodaty H, Low LF. A tiered model of psychogeriatric service delivery: An evidence-based approach. *Int J Geriatr Psychiatry* 2006;21:645–53.
2. Howe EG. Update on Alzheimer's disease: A shift in the paradigm of treatment. *Psychiatry* 2006;3(11):24–36.
3. Waldemar G, Dubois B, Emre M, et al. Recommendations for the diagnosis and management of Alzheimer's disease and other disorders associated with dementia: EFNS guideline. *Eur J Neur* 2007;14:e1–26.
4. Royall DR, et al. High dose sertraline improves executive function in vascular cognitive impairment. International Society for Vascular and Cognitive Disorders Annual Meeting, July 11–14, San Antonio, Texas, Final Program. Abstract P-124. Available at: [www.medpagetoday.com/tbprint2.cfm?tbid=6161&topicid=146](http://www.medpagetoday.com/tbprint2.cfm?tbid=6161&topicid=146). Accessed 7/17/2007.
5. Cascade EF, Kalali AH, Citrome L. Antipsychotic use varies by patient age. *Psychiatry* 2007;4:20–1.
6. Lyketsos CG, Olin J. Depression in Alzheimer's disease: Overview and treatment. *Biol Psychiatry* 2002;52:243–52.
7. Thompson S, Herrmann N, Rapoport MJ, et al. Efficacy and safety of antidepressants for treatment of depression in Alzheimer's disease: A meta-analysis. *Can J Psychiatry* 2007;52:248–559.
8. Patter GG, Stiffens DC. Contribution of depression to cognitive impairment and dementia in older adults. *Neurologist* 2007;13:105–17.
9. Wilson RS, Schneider JA, Boyle PA, et al. Chronic distress and incidence of mild cognitive impairment. *Neurology* 2007;68:2085–92.
10. Buhr G, White H. Difficult behaviors in long-term care patients with dementia. *J Am Med Dir Assoc* 2007;8:e101–3.
11. Hermann N, Lanctot KL, Rothenburg LS, et al. A placebo-controlled trial of valproate for agitation and aggression in Alzheimer's disease. *Dement Geriatr Cogn Disord* 2007;23:116–9.
12. Tariot PN, Raman R, Jakimovich L, et al. Divalproex sodium in nursing home residents with possible or probable Alzheimer Disease complicated by agitation: A randomized, controlled trial. *Am J Geriatr Psychiatry* 2005;13:942–89.
13. Howe, EG. Do we undervalue the feelings of patients with cognitive impairment? *J Clin Ethics* 2006;17:291–301.
14. Conn D, Thorpe L. Assessment of behavioural and psychological symptoms associated with dementia. *Can J Neurol Sci* 2007;34(Suppl 1):S 67–71.
15. Annerstadt L, Elmstahl S, Ingrad B, et al. Family caregiving in dementia—an analysis of the caregiver's burden and the "breaking-point" when home care becomes inadequate. *Scand J Public Health* 2000;28:23–31.
16. Callahan CM, Boustani MA, Unverzagt FW, et al. Effectiveness of collaborative care for older adults with Alzheimer disease in primary care. *JAMA* 2006;295:2148–57.
17. Dubois B, Feldman HH, Jacova C, et al. Research criteria for the diagnosis of Alzheimer's disease: Revising the NINCDS-ADRDA criteria. *Lancet Neurol* 2007;6:734–46.
18. Foster N. A new framework for the diagnosis of Alzheimer's disease. *Lancet Neurol* 2007;6:667–9. ●